

## PCT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year) 12 July 2001 (12.07.01)	
International application No. PCT/US00/20007	Applicant's or agent's file reference 126745200641
International filing date (day/month/year) 21 July 2000 (21.07.00)	Priority date (day/month/year) 22 July 1999 (22.07.99)
Applicant SHEPARD, H., Michael	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 20 February 2001 (20.02.01)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Nestor Santesso Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>126745200641</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/ 20007</b>	International filing date (day/month/year) <b>21/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>22/07/1999</b>
Applicant <b>NEWBIOTICS, INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-18 and 20-25 in part

Present claims 1-19 relate to a method defined by reference to a set of desirable characteristics or properties, related to the pharmacological profile of the prodrug to be used.

The claims cover all methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only one single prodrug. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the prodrug by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Unfortunately, this lack of support, disclosure and clarity is not overcome by the structural formulae of claims 2-3.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the prodrug for which pharmacological data were provided.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/20007

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
W0 0033888	A	15-06-2000	AU	2373300 A	26-06-2000
W0 9906072	A	11-02-1999	NONE		
W0 9512678	A	11-05-1995	AU	690935 B	07-05-1998
			AU	8065794 A	23-05-1995
			CA	2175687 A	11-05-1995
			EP	0725826 A	14-08-1996
			JP	9505037 T	20-05-1997
			NZ	275147 A	24-11-1997
			US	5958682 A	28-09-1999
W0 0107087	A	01-02-2001	AU	6231800 A	13-02-2001
			AU	6358900 A	13-02-2001
			WO	0107088 A	01-02-2001
W0 9937753	A	29-07-1999	AU	2464699 A	09-08-1999
			BR	9907736 A	17-10-2000
			CN	1291228 T	11-04-2001
			EP	1045897 A	25-10-2000
			US	6245750 B	12-06-2001

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20007

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 A61K47/48 A61P35/00 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, CANCERLIT, DISSERTATION ABS, EMBASE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 00 33888 A (DUBOIS VINCENT ;TROUET ANDRE (BE); FERNANDEZ ANNE MARIE (BE); COUL) 15 June 2000 (2000-06-15) page 8, line 6 - line 14 example 1	1-25
X	WO 99 06072 A (BOEHRINGER MANNHEIM CORP ;POWELL MICHAEL J (US)) 11 February 1999 (1999-02-11) page 9, line 5 -page 10, line 5 page 15, line 3 - line 17 -/--	1-25



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

3 July 2001

Date of mailing of the international search report

17/07/2001

Name and mailing address of the ISA

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Authorized officer

Dullaart, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20007

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NICULESCU-DUVAZ I ET AL: "GENE-DIRECTED ENZYME PRODRUG THERAPY: A REVIEW OF ENZYME/PRODRUG COMBINATIONS" EXPERT OPINION ON INVESTIGATIONAL DRUGS,GB,ASHLEY PUBLICATIONS LTD., LONDON, vol. 6, no. 6, 1997, pages 685-703, XP000901460 ISSN: 1354-3784 schemes tables ---	1-25
Y	BAGSHAW K D: "ANTIBODY-DIRECTED ENZYME PRODRUG THERAPY: A REVIEW" DRUG DEVELOPMENT RESEARCH,US,NEW YORK, NY, vol. 34, no. 2, 1 February 1995 (1995-02-01), pages 220-230, XP000562092 ISSN: 0272-4391 page 223; table 1 page 224, right-hand column, last paragraph -page 226, left-hand column ---	1-25
Y	MELTON ET AL: "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" DRUGS OF THE FUTURE,ES,BARCELONA, vol. 21, no. 2, 1996, pages 167-181, XP002080157 ISSN: 0377-8282 table 1 figures 2,4-9,11,13-16 page 178, paragraph CONCLUSIONS ---	1-25
Y	WOLFE L A ET AL: "ANTIBODY-DIRECTED ENZYME PRODRUG THERAPY WITH THE T268G MUTANT OF HUMAN CARBOXYPEPTIDASE A1: IN VITRO AND IN VIVO STUDIES WITH PRODRUGS OF METHOTREXATE AND THE THYMIDYLATE SYNTHASE INHIBITORS GW1031 AND GW1843" BIOCONJUGATE CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY, WASHINGTON, vol. 10, no. 1, January 1999 (1999-01), pages 38-48, XP000800838 ISSN: 1043-1802 abstract figures tables --- -/--	1-25

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20007

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GRIENGL H ET AL: "PHOSPHONOFORMATE AND PHOSPHONOACETATE DERIVATIVES OF 5-SUBSTITUTED 2'DEOXYURIDINES: SYNTHESIS AND ANTIVIRAL ACTIVITY" JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 31, no. 9, 1988, pages 1831-1839, XP002036743 ISSN: 0022-2623 abstract page 1833 -page 1834 ---	1-25
Y	MCGUIGAN C ET AL: "ARYL PHOSPHORAMIDATE DERIVATIVES OF D4T HAVE IMPROVED ANTI-HIV EFFICACY IN TISSUE CULTURE AND MAY ACT BY THE GENERATION OF A NOVEL INTRACELLULAR METABOLITE" JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 39, no. 8, 1996, pages 1748-1753, XP000578130 ISSN: 0022-2623 abstract page 1748, paragraph INTRODUCTION table ---	1-25
Y	WO 95 12678 A (CONNORS THOMAS ;KNOX RICHARD (GB); SHERWOOD ROGER (GB); CANCER RES) 11 May 1995 (1995-05-11) examples claims ---	1-25
E	WO 01 07087 A (SHEPARD H MICHAEL ;NEWBIOTICS INC (US)) 1 February 2001 (2001-02-01) the whole document ---	1-25
Y,P	WILDNER OLIVER ET AL: "Enzyme prodrug gene therapy: Synergistic use of the herpes simplex virus-cellular thymidine kinase/ganciclovir system and thymidylate synthase inhibitors for the treatment of colon cancer." CANCER RESEARCH, vol. 59, no. 20, 15 October 1999 (1999-10-15), pages 5233-5238, XP001002739 ISSN: 0008-5472 abstract figure 1 page 5236, paragraph DISCUSSION -page 5237 --- -/--	1-25

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20007

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KUMAR A ET AL: "SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME CYCLIC PHOSPHORAMIDATE NUCLEOSIDE DERIVATIVES" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 9, 1990, pages 2368-2375, XP002171072 ISSN: 0022-2623 abstract schemes figures tables page 2371, left-hand column, last paragraph -page 2372, right-hand column, line 3	1-25
Y	----- FARROW S N ET AL: "SYNTHESIS AND BIOLOGICAL PROPERTIES OF NOVEL PHOSPHOTRIESTERS A NEW APPROACH TO THE INTRODUCTION OF BIOLOGICALLY ACTIVE NUCLEOTIDES INTO CELLS" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 5, 1990, pages 1400-1406, XP002171073 ISSN: 0022-2623 the whole document	1-25
P,X	----- WO 99 37753 A (GROZIAK MICHAEL P ;SHEPARD H MICHAEL (US); NEWBIOTICS INC (US)) 29 July 1999 (1999-07-29) the whole document -----	1-25